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Life cycle assessment in green chemistry: overview of key parameters and methodological concerns

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Abstract
Purpose Several articles within the area of green chemistry often promote new techniques or products as 'green' or 'more environmentally benign' than their conventional counterpart although these articles often do not quantitatively assess the environmental performance. In order to do this, life cycle assessment (LCA) is a valuable methodology. However, on the planning stage, a full-scale LCA is considered to be too time consuming and complicated. Two reasons for this have been recognised, the method is too comprehensive and it is hard to find inventory data. In this review, key parameters are presented with the purpose to reduce the time-consuming steps in LCA.
Methods In this review, several LCAs of so-called 'green chemicals' are analysed and key parameters and methodological concerns are identified. Further, some conclusions on the environmental performance of chemicals were drawn.
Results and discussion For fossil-based platform chemicals several LCAs exists but for chemicals produced with industrial biotechnology or from renewable resources the number of LCAs is limited, with the exception of biofuels, for which a large number of studies are made. In the review, a significant difference in the environmental performance of bulk and fine chemicals was identified. The environmental performance of bulk chemicals are closely connected to the production of the raw material and thereby different land use aspects. Here, a lot can be learnt from biofuel LCAs. In many of the reviewed articles focusing on bulk chemicals a comparison regarding fossil and renewable raw material was done. In most of the comparisons the renewable alternative turned out to be more environmentally preferable, especially for the impact on GWP and energy use. However, some environmental concerns were identified as important to include to assess overall environmental concern, for example eutrophication and the use of land.
Conclusions To assess the environmental performance of green chemicals, quantitative methods are needed. For this purpose, both simple metrics and more comprehensive methods have been developed, one recognised method being LCA. However, this method is often too time consuming to be valuable in the process planning stage. This is partly due to a lack of available inventory data, but also because the method itself is too comprehensive. Here, key parameters for the environmental performance and methodological concerns were described to facilitate a faster and simpler use of LCA of green chemicals in the future.

Keywords Biocatalysis · Bulk chemicals · Fine chemicals · GHG · LCA · Renewable resources · Simplified LCA · Sustainable chemistry · Yield

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1 Introduction

As a response to the general growing concern for pollution, greenhouse gas emissions and other effects on the environment the chemical industry is today making real efforts to achieve more sustainable products and production processes. To help the development of a sustainable chemical industry, concept such as 'green chemistry' was launched—targeted at making chemical processes and products 'green by design'

(Anastas and Warner 1998). As a consequence, many new technologies are marketed by industry and academia as 'green' based on the fact that they fulfil one or several of the green chemistry principles. However, the principles are qualitative and do not per se guarantee significant environmental benefits in quantitative terms. Hence quantitative evaluation methods are needed to justify the claimed environmental benefits (Winterton 2001).

To date several different approaches to quantify the environmental performance of chemical products and processes have been developed. For instance, life cycle assessment (LCA) is a methodology widely used by government institutions, academia and industrial companies to quantify a product's or process' entire environmental impact, from raw material production, manufacturing, use and disposal, i.e. from cradle-to-grave. Different categories are used to compare the impact on different areas of environmental concerns (e.g. global warming, release of toxic compounds and eutrophication). LCA has indeed been recognised as a valuable tool to compare conventional production methods with 'green chemistry' methods for producing chemicals (OECD 2001; Anastas and Lankey 2000; Azapagic 2002). However, due to the extensive need for input data (inventory data), LCA is best adapted to compare products and processes that are already in use. At the research or development stage of a new product or process, conducting a full-scale LCA is often thought of as too difficult and time consuming (Koller et al. 2000) and indeed may prove inaccurate. Instead, more simple models or environmental metrics are often being used as a comparative basis. On the other hand, this approach has been criticised for being misleading and possibly leading to sub-optimization.

In this paper, the use of these different tools for assessing and guiding the development of new products and processes will be reviewed and discussed with respect to when and how they should be applied in different stages of development. In this article, a special emphasis is given to the use of biocatalysis and to the use of renewable resources, both widely claimed to generate 'green' processes or products. This article also aims to provide guidance in the identification of key parameters affecting the environmental performance of different types of chemicals and processes and to discuss the main methodological concerns. Further, an extensive list of references to published LCAs is given to serve as a potential source of life cycle inventory (LCI) data.

1.1 Environmental metrics

Environmental metrics are values calculated from a single defined equation often based on the reaction's stoichiometry, or variations thereof. Examples of *metrics* used are the *E-factor* (Sheldon 1992) which is defined by the amount of waste created per kilogramme of product, *atom economy* (Trost 1991) that measures how much of the reactants that end up in the final product, *effective mass yield* (Hudlicky et al. 1999) where the mass of the desired product relative to the mass of all non-benign materials is calculated, and *C-factor*, which is defined as the mass ratio of the CO_2 to product mass (Voss et al. 2009).

Also companies have developed their own metrics. One example is the *carbon efficiency* that measures the amount of carbon in the final product compared to the carbon in the reactants and another is the *reaction mass efficiency* that is based on atom economy and yield, both developed by GlaxoSmithKline (GSK) (Curzons et al. 2001). An evaluation of different green chemistry metrics has previously been made by Constable et al. (2002) who compared different metrics currently available, with the goal of designing a metric set suitable for GSK.

The merit of using the *metrics* is that they are simple to use and give instant feedback to a change to the process or the reaction pathway and can therefore easily be used for modelling or *what-if* analysis. However, a drawback is that the same weight is given to all different types of waste generated, i.e. 1 kg of sodium chloride is equated to 1 kg of organic solvent. For example in a LCA of a pharmaceutical compound, biocatalytical processes scored better concerning greenhouse gas (GHG) emissions and energy consumption but resulted in a higher E-factor than its conventional counterpart (Henderson et al. 2008). An even more serious weakness, however, is that the output is relevant only for one environmental impact category, e.g. waste generation, taking no consideration of the multi-dimensional nature of the environmental problems and there is therefore a serious risk of sub-optimization, i.e. reductions in waste volumes are exchanged for carbon dioxide emissions, etc.

1.2 Simple models

An added level of complexity is used in the s*imple models.* They are based on multiple input variables and commonly use knowledge about the process and reactants to rate it. A number of such computer models to evaluate the environmental performance of a product or process have been developed. One example is EcoScale developed to evaluate both economical and ecological parameters of organic synthesis (van Aken et al. 2006). However, the model is based on subjective rating of different parameters and should probably be considered as a qualitative assessment although the output is quantified. Another model is EATOS (Eissen and Metzger 2002) developed as a tool to compare different routes in organic synthesis. The model considers all of the common environmental impacts and weighs the input material according to a given scheme based on their performance, e.g. CO_2 emission per kilogramme of material. However, the EATOS database only contains a very limited

number of chemicals (around 60) and also lack inventory data for many of the compounds, in the absence of which the impact is estimated based on the cost of the chemical. The method is highly questionable, especially when comparing fossil-based chemicals with chemicals from renewable resources. For EATOS to be a valuable tool a more extensive database is required and thus does not offer any significant benefits over a full-scale LCA study.

1.3 Life cycle assessment

The LCA methodology is defined by the ISO 14040 standard (ISO, 2006) and is divided in four phases: the *goal and scope definition*, *inventory analysis*, impact *assessment* and *interpretation*. In the goal and scope definition, the product or process studied and the purpose of the study is described. The standard stresses that the goal and scope must be clearly defined and also consistent with the intended application (ISO 2006). In the inventory analysis, all inventory data is collected to then be 'processed' in the impact assessment and finally evaluated during the interpretation phase.

Several companies have developed modified *in-house* LCA methods, based on the guidelines in the ISO standard, for evaluating the sustainability of chemicals and chemical reactions. For example, the fine and pharma chemical producer, GlaxoSmithKline, has developed the FLASC-tool to systematically evaluate synthetic organic reactions and processes (Curzons et al. 2007). BASF has similarly developed the 'Eco-efficiency Analysis' method (Saling et al. 2002; Kicherer et al. 2007) that aims to identify the most economically efficient environmental improvements. Both companies have published several scientific papers describing both methods and also case studies on their products (GSK (Jiménez-González 2004; Henderson et al. 2008; Wernet et al. 2010), BASF (Saling et al. 2002; Kicherer et al. 2007)).

2 Results and discussion

2.1 Review of LCAs of chemicals

Chemicals are often categorised based on production volume, functionality and price, ranging from bulk to speciality to fine chemicals (and pharmaceuticals). Fine chemicals are high-value chemicals produced in small to moderate quantities for specialised applications, for example vitamins, pesticides or building blocks for pharmaceuticals, whereas bulk chemicals often are low-value products such as solvents or polymeric monomers (and even fuels) produced in large quantities. Due to the different ways these are produced in terms of process intensity, degree of optimization, the environmental aspects and issues as well as the key parameters for each segment are different. For instance, because of the more complex chemistry often involving many steps, fine chemicals normally generate more waste during production than bulk chemicals and involve a higher Cumulative Energy Demand.

The most relevant parameters influencing the environmental performance and the most important methodological concerns affecting the results of the studies of each category have been identified and are discussed below. In Table 1, some of the reviewed articles are presented together with a short description of their content. These articles can also help in the search for inventory data for different products or processes.

From the review of these studies, some general observations were made: The number of available LCAs of chemicals is rather limited, especially for fine chemicals. For fossil-based platform chemicals, several LCAs exist, for example in the Ecoinvent database (Ecoinvent 2010). For chemicals produced with industrial biotechnology or from renewable resources, the number of LCAs is very limited, with the exception of biofuels, for which a large number of studies are made. One of the reasons is probably the greater methodological difficulty involved in assessing the production of renewable raw materials such as biomass (OECD 1998).

Within the fine chemicals segment, lots of research are being directed at developing new processes but these are rarely based on renewable resources or using bioprocesses. In this review, some of these have still been included due to their importance in identifying key parameters. For renewable bulk chemicals, many parallels can be drawn from LCAs of biofuels where lots of attention recently have been put on identifying key parameters in the raw material production, and therefore some articles on biofuel were also included in the review. When reviewing the articles, focus was on identifying important parameters, but some conclusions on the environmental performance of chemicals can also be drawn and these are presented in the final chapter.

2.2 Methodological concerns

Below methodological concerns are discussed, based on the findings from the review.

2.2.1 Functional unit

It is important that the functional unit is defined correctly, quantitatively, qualitatively and in time. This is crucial when comparing two products as the functional unit is then used as the basis of comparison (Baumann and Tillman 2004). As an example, in an LCA for different wood coatings, Gustafsson and Börjesson (2007) have a functional unit including both the area of application and the life-time of a treatment, since both these parameters are needed to

Table 1 Reviewed studies on renewable chemicals or chemicals produced using biotechnical production methods

Reference	Description
Biofuels and land use	
Ahlgren et al. (2009)	GHG emissions from cultivation of crops for biofuel following EU Directive 2009/28/EC, land use
Börjesson and Tufvesson (2010)	LCA on crop-based biofuels, cradle-to-gate, land use
Cherubini et al. (2010)	LCA of biofuels, key issues, recommendations
Cherubini (2010)	Bioenergy systems, GHG, key parameters, methodological concerns
Concawe, EUCAR (2007)	LCA of biofuels, well-to-wheel
Fargione et al. (2008)	Land use change, biofuel carbon debt
Gnansousounou et al. (2009)	LCA of biofuels, energy, GHG, some method concerns
Kim et al. (2009b)	Biofuels, land use change
Searchinger et al. (2008)	Direct and indirect land use change
Müller-Venk and Brandâo (2010)	Land use in LCA
Kløverpris et al. (2010)	Land use, marginal land
Zilberman et al. (2010)	Criticism including indirect land use in LCA modelling
European Commission (2009)	Directive 2009/28/EC on the promotion of the use of energy from renewable resources
IPCC (2006)	Method to include nitrous oxide emissions from soil in LCA
Biorefinery concept	
Cherubini and Jungmeier (2010)	LCA of biorefinery producing ethanol, energy and chemicals, land use
Cherubini and Ulgiati (2010)	LCA of biorefinery using crop residues
Kamm and Kamm (2004)	Review of biorefinery articles describing different types of biorefineries
Biopolymers	
Akiyama et al. (2003)	LCA from cradle-to-gate of PHA from renewable resources by fermentation vs. LDPE HDPE PP and PS
BREW (2006)	LCA from cradle-to-grave (gate) of 21 different renewable bulk chemicals compared to their fossil counterparts
Dornburg et al. (2008)	Scenario projections for future bio-based bulk chemicals (PHA, PTT, PLA, ethyl lactate, ethylene, succinic acid, apipic acid, acetic acid and *n*-butanol)
Gross and Kalra (2002)	Biodegradable polymers
Harding et al. (2007)	LCA from cradle-to-gate of biologically based PHB vs, fossil PP and PE
Hermann and Patel (2007)	Methodology to technically and economically evaluate present and future production routs of bio-based chemicals
Heyde (1998)	LCA of biodegradable polymer produced from PHB, focus on energy and GWP and compared with fossil PE and PS
Kim and Dale (2005)	LCA from cradle-to-gate of PHA produced from corn using fermentation
Madival et al. (2009)	LCA from cradle-to-grave of bio-based PLA vs. fossil PET and PS for use as clamshell containers
PRO-BIP (2004)	Evaluation of bio-based polymers (technology-economy-enironment) in Europe produced in large scale
Roes and Patel (2007)	LCA from cradle-to-grave of bio-based PTT, PHA, PET, PE and ethanol compared to the petrochemical processes
Shen and Patel (2008)	Review. LCA of polysaccharide materials
Urban and Baksi (2009)	LCA of bio-based and fossil 1,3-propanediol using three different LCA techniques
Vink et al. (2003)	LCA from cradle-to-gate of bio-based NatureWorks® PLA vs. fossil polymers
Vink et al. (2007)	LCA from cradle-to-gate of NatureWorks® PLA, present and future
Vink et al. (2010)	Eco-profile for Ingeo PLA production by NatureWorks®
Weiss et al. (2007)	Environmental performance of 45 bio-based energy, fuels and materials compared to their conventional counterpart
Weiss and Patel (2006)	Comparison of different LCAs on energy, fuels and material
Lubricants	
Ekman and Börjesson (2010)	LCA of lubricants based on renewable resources produced using biocatalysis
Willing (2001)	Lubricants based on renewable resources, oleochemical esters
Surfactants	
Adlercreutz et al. (2010)	Techno-economic evaluation of alkanolamide biosurfactants produced using biocatalytic and conventional methods

Table 1 (continued)

Reference	Description
Patel (2004)	Renewable surfactants, energy and GHG saving potentials
Saouter et al. (2006)	LCA of oleochemical and petrochemical surfactants
Fatty acid esters	
Petersson et al. (2005)	Energy assessment of fatty acid production, biocatalytic vs. conventional production. Gate-to-gate
Tufvesson and Börjesson (2008)	LCA from cradle-to-grave of renewable and fossil product
Hills (2003)	Energy assessment from gate-to-gate for biocatalytically produced fatty acid esters
Thum and Oxenbøll (2006)	LCA from gate-to-gate of cosmetic ester oils produced using biocatalytic and conventional production processes
Martinez (2005)	LCA from gate-to-gate of fatty acid esters
Gustafsson and Börjesson (2007)	LCA of industrial wood surface coatings, one based on bio-based fatty acid ester
Fine chemicals	
Saling and Kicherer (2006)	Eco-efficiency analysis of the dye indigo and vitamin B2 produced using biotechnology
Pharmaceuticals	
Bruggink and Nossin (2006)	LCA of bio-based routes to cephalexin
Henderson et al. (2008)	LCA from cradle-to-gate of 7-ACA, biocatalytic vs. chemical synthesis
Wernet et al. (2010)	LCA from cradle-to-gate of API
Jiménez-Gonzàlez et al. (2004)	LCA from cradle-to-gate of a typical API
Jödicke et al. (1999)	LCA from cradle-to-gate of enantioselective reductions. Biocatalytic vs. conventional catalyst
Ponder and Overcash (2010)	LCI from gate-to-gate of vancomycin hydrochloride
Enzymes	
Nielsen et al. (2007)	LCA from cradle-to-gate of five different enzyme products
Kim et al. (2009a)	LCA from cradle-to-gate for three different enzymes for pharmapplication
Fossil resources	
Ecoinvent (2010)	Database for LCI data
APME (2010)	Bulk, Different chemicals and plastics from fossil resources, Cradle-to-gate
Hischier et al. (2004)	Method for establishing LCIs for chemicals in Ecoinvent
Kirk-Othmer (2010)	Encyclopaedia of chemical technology
McKetta (1976)	Encyclopaedia of chemical processing and design
Ullmann's Encyclopedia of Industrial Chemistry (2006)	Chemical dictionary
Wernet et al. (2009)	Modelling environmental impact of fine and basic chemicals based on molecular structure
Solvents	
Blowers and Titus (2004)	LCI for $scCO_2$
Capello et al. (2009)	Petrochemical solvent production, 40 new LCI established
Curzon et al. (1999)	Solvent selection guide, 35 solvents
Gani et al. (2005)	Method for selection of solvents
Gani et al. (2008)	Multi-step reaction systems
Hellweg et al. (2004)	LCA from cradle-to-gate of 13 different solvents
Sheldon (2005)	Review, solvents for sustainable synthesis
LCA of chemicals – general	
Klöpffer (2005)	Modelling LCA for chemicals and chemical production
Herrchen and Klein (2000)	LCA to evaluate production processes
Millet et al. (2007)	LCA as a method to use on the planning stage
Azapagic (2002)	
Anastas and Lankey (2000)	The use of LCA in green chemistry
Lankey and Anastas (2002)	The use of LCA in green chemistry
Sustainable chemistry	
Steinhäuser et al. (2004)	How do we achieve a sustainable chemistry?
Wilke and Vorlop (2004)	Review, bioconversion of renewable resources vs. conventional chemistry

Table 1 (continued)

Reference	Description
Woodley (2008)	Review, using biocatalysis in pharmaceutical processes
Pollard and Woodley (2006)	Review, using biocatalysis in pharmaceutical processes
Tucker (2006)	Pharmaceuticals and green chemistry—concept article
Jiménez-Gonzàlez et al. (2000)	Guidance in selecting environmentally preferable technology in the pharmaceutical industry
Schmidt et al. (2001)	Review. Possibilities with the use of biocatalysis
Azapagic et al. (2006)	A method for including sustainability (LCA) into process design
Dale (2003)	Using renewable raw material in the chemical industry
LCA method	
Jiménez-Gonzàlez et al. (2000)	Model for developing gate-to-gate LCI information
Curzons et al. (2007)	Description of the FLASC-tool developed by GSK
Kicherer et al. (2007)	LCA and LCC—Eco-efficiency by BASF
Saling et al. (2002)	Eco-efficiency analysis—method, developed by BASF

describe the function of a wood coating, as different coatings require different amounts of material and are worn out after different times. Similar discussions are found in various fields. For biofuels, it has been advocated that the functional unit should be expressed both per megajoules of biofuels but also per hectare and year (Cherubini et al. 2009), whereas Geisler et al. (2005) discuss the use of different functional units for pesticide production.

2.2.2 System definition and boundaries

Materials are widely studied LCAs and parallels can be drawn from these on how to assess chemicals in LCA (Klöpffer 2005). Klöpffer identifies important cases how to handle system boundaries in LCA, where one case is identified as suitable for 'green chemistry'. This case is when there are different production routes and/or raw materials for manufacturing the same substance(s). In this case, comparison is possible on the basis of cradle-to-factory gate. Also, including the disposal phase, or 'grave', is important for including carbon dioxide from photosynthesis, the advantage of using renewables. One must compare two products with all process steps included; some studies only compare the production process and exclude post-treatment steps leading to misleading results. When comparing biocatalytic and conventional production, the advantages of the biocatalytic process are often found in the less number of post-treatment steps needed.

To conclude, for bulk chemicals, it is easier to do cradle-to-grave investigations, but for fine chemicals and pharmaceuticals, it is often more relevant to only do cradle-to-factory gate investigations. This is so since the chemicals often end up in different applications with different end-of-life scenarios. However, it is important to also include the post-treatment steps that are needed after the production process to get a reliable result.

2.2.3 Allocation method

Allocation refers to the distribution of environmental burdens between co-products in the LCA of multifunctional systems. The allocation can be based either on a physical property of the process stream, e.g. based on mass or energy content of the products, or based on the value of the process streams called economic allocation. The ISO 14040 recommends avoiding allocation whenever possible (ISO 2006), either through division of the whole process into subprocess related to co-products or by expanding the system boundaries to include the additional functions related to them, often referred to as system expansion. In biofuel production systems, the choice of allocation method has been found to be one of the parameters that affect the results the most (e.g., Börjesson and Tufvesson (2010)). In many of the reviewed LCAs, physical allocation was chosen, whereas in some, the result was presented for both physical and economical allocation (Tufvesson and Börjesson 2008).

The most reliable result is probably obtained when system expansion is used, but it also requires additional inventory data and thus more time. Further a choice regarding what system is being replaced affects the result and aspects regarding how much of a product that can be replaced also becomes important. The increased uncertainty when involving more inventory data must also be taken into account. For physical allocation, the basis of the allocation is independent of time but no consideration is made regarding the quality of the different products. For instance, this allocation method would clearly be misleading in chemical processes where by-product streams with very low value (more or less considered as waste) would equally share the environmental burden of the desired product. This is especially important to consider for fine chemicals and pharmaceuticals where waste streams are big and the added value in each process step is large. One concern regarding economical allocation

is that prices vary over time. However, price on all raw materials are often closely connected and a higher price on one raw material often affects also other materials (Börjesson and Tufvesson 2010).

We recommend presenting the results using different allocation methods, or discussing how the result will be affected if another allocation method is chosen. For bulk chemicals, we recommend system expansion since it is important to include the benefits from the by-products from cultivation and processing. For fine chemicals, the use of economic allocation is recommended since the by-products carry a relatively low value compared to the main product.

2.2.4 Reference system

Since the functional unit of the studied system normally is unique for the studied system (see above), the results do not say so much in themselves and thus a reference system is needed towards which the process or product is compared. For biofuels, the reference system is often a fossil fuel. However, sometime even then the picture is not complete; in case of system expansion, a reference substitute product must also be defined, for example rape meal replacing soy meal for animal feed in RME production. For pharmaceuticals, a new drug being developed is often not possible to compare with existing ones on the market due to differences in quality and optimisation, complicating the choice of a good reference case.

2.2.5 State of the art vs. emerging technologies

In the reviewed articles, many times, well-established optimised conventional techniques were compared with biocatalytic processes, not yet fully optimised, something that can give misleading results. Still, there is a need to do environmental evaluations on early planning stages. This can be done by establishing multiple cases—for instance one state-of-the-art biocatalytic production and one representing a potential future improved production process. When studying emerging technologies, such as newly developed biotechnical production processes, it is important to consider the fast changes in technical development over time and make use of the latest inventory data available.

2.2.6 Choice of environmental impact categories

In recent years, the environmental problem obtaining most media attention is global warming. However, the importance of the different impact categories (which each represents different environmental issues) varies depending on which type of chemical is being evaluated. For biofuels and bulk chemicals, energy and global warming potential (GWP) indeed is important but also eutrophication and parameters connected to the cultivation (soil parameters, water usage, biodiversity, etc.) are of importance. On the other hand, for fine chemicals, other impact categories such as use of toxic chemicals and emissions of volatile organic compounds from the use of solvents should perhaps be of greater concern. Relative to the emissions to climate change from the transportation and energy sector, the contribution from the production of fine chemicals and pharmaceuticals is surely modest.

For fine chemicals, the assessment of toxicity often leads to difficulties. Several characterisation methods for dealing with toxicity in LCA have been developed. One is USES (also referred to as CML2001) (Huijbregts et al. 2000a; Huijbregts et al. 2000b; Huijbregts et al. 2000c) and another is EDIP97 (Wenzel et al. 1997). Even so, quantification of toxicity is difficult, mainly because of two reasons. One is the lack of detailed inventory data and the other is that there is no coherent framework on how to evaluate the toxicity of chemicals (Baumann and Tillman 2004). A problem is that the models often emphasise different types of emissions leading to diverging results depending on which method chosen (Gustafsson and Börjesson 2007), even though this will probably be overcome with time through efforts such as the OMNIITOX (operational models and information tools industrial applications of eco/toxicological impact assessments) project. This project is funded under a EU 5th Framework Programme aiming at developing characterisation factors for assessing the potential toxic impacts of chemicals within the framework of LCA (Molander et al. 2004; Carlson et al. 2004; Olsen et al. 2003). Also, the enforcement of the new REACH legislation (European Commission 2006), where LCA have been pointed out as having a future role in chemical regulation, might help in overcoming this problem.

We recommend that to get an accurate result regarding the environmental performance of chemicals, relevant impact categories must be included in the study.

2.3 Raw material production

In previous LCAs, the production of biomass has been recognised as the main contributor the environmental impact of biofuels (Börjesson and Tufvesson 2010). In the review, it was concluded that this most often is the case also for bulk chemicals. Below, important key parameters are presented and recommendations are given on how to handle these aspects in LCA.

2.3.1 Fossil resources

Conventionally, LCAs have been conducted on products made from fossil raw materials and several platform and base chemicals are well covered (Ecoinvent 2010). In

Wernet et al. (2009), a model to predict LCI data for 338 petrochemicals were presented, and in Hischier et al. (2004), a method (called the Ecoinvent method) is presented to calculate the environmental performance of chemicals using for example production energy data from reference literature (e.g. Ullman's Encyclopedia of Industrial Chemistry; Ullmann's Encyclopedia of Industrial Chemistry 2006) or other similar sources (e.g. Kirk-Othmer 2010; McKetta 1976). In the Ecoinvent database, also inventory data for several petrochemicals are included (Ecoinvent 2010). Inventory data for fossil-based products is therefore more easily available than for products made from renewable resources.

2.3.2 Renewable resources

For the production of renewable raw material, several parameters affecting the environmental performance makes the calculations more complex. For the production of chemicals based on biomass resources, only a few studies take all these parameters into account. However for biofuels, much work has been done, identifying both important parameters as well as methodological concerns affecting the result. These results are also applicable for bulk and speciality chemicals, where the impact from the raw material production is significant. The important parameters are emissions of N_2O from both fertiliser production and from agricultural land, crop residue removal and direct and indirect land use change.

The greenhouse gas emissions of N_2O are an important parameter for raw material produced from cultivation, especially for annual crops with higher fertilisation rates than perennial crops. Emissions of N_2O originate from both production of fertilisers but also from decomposition of organic matter in soil (Tufvesson and Börjesson 2008). The emissions of N_2O from production of fertilisers are however decreasing due to implementation of catalytic cleaning in the fertiliser production plants (Börjesson and Tufvesson 2010).

The emissions N_2O from agricultural land varies depending on soil type, climate, crop, and tillage method and fertiliser application rate (Bernesson et al. 2006, Bouwman et al. 2002; Nevison et al. 1996). The emissions from soils have been discussed in recent years and different calculation methods have been developed giving diverging results (Kendall and Chang 2009). The method recommended by the EC Directive is the IPCC model (European Commission, 2009), calculating direct and indirect emissions of N_2O based on the assumption of a linear relationship between input of nitrogen and N_2O emissions (IPCC 2006).

The incentives of removing crop residues, such as straw, are mainly the possibility of using the straw as animal fodder or to be combusted in a combined heat and power plant replacing other sources of energy. However, removing the straw from the field results in slightly more tractor operations and it also affect N_2O emissions, leaching of nitrate and changes in soil carbon pools. However, if the straw is replacing a fossil source of energy, it leads to climate change benefits, compared to if the straw is left in the field (Börjesson and Tufvesson 2010).

Direct land use change may occur when the cultivation system is changed on a specific land area, thereby generating possible changes to the carbon stock of that land. One example is conversion of forest land to agricultural land. Direct land use change can be both a benefit and a disadvantage, depending on the earlier use of the land. For example, perennial grasses replacing annual crops may increase the carbon sequestration. Consequently, the previous state of the land use can significantly affect the GHG balance of the investigated product.

Indirect land use change, ILUC, may occur when land currently used for feed or food crop production is changed into bioenergy or chemical production and the demand for the previous land use remains; the displaced agricultural production will move over to other places. The issue of ILUC is a controversy and the importance of this in the production of biofuels has been investigated in some recent studies (see, Searchinger et al. 2008; Fargione et al. 2008; Gallagher 2008), which conclude that potential displacement of food and feed production may completely 'off-set' the GHG gas benefits for biofuels. The argue against ILUC being included in LCA is that it contradicts the basic principle of regulation—that one can only be responsible for actions that one can control (Zilberman et al. 2010). Another problem with including ILUC is that it is difficult to estimate and varies over time (Gallagher 2008; Ravindranath et al. 2009; Kim and Dale 2009). Thus, a conclusion is that ILUC have to be recognised in conjunction with the expansion of biofuel and biochemical production, but there is no reliable, scientific methodology available today to include these aspects in LCA today (Kim and Dale 2009).

We recommend that when developing production systems for biofuels and bulk chemicals, it is important to evaluate factors such as area efficiency, which is the amount of raw material produced from crops harvested from a certain area. This can easily be included in LCAs by changing the functional unit and thereby indirectly evaluate the differences in land use efficiency between different production systems. It is also important to include all the other key parameters described above in the calculations.

2.4 Production process

As well as for the production of biomass, a number of key parameters identified for the chemical process are also very important to include when doing LCAs. These are listed below.

2.4.1 Yield

The yield of a reaction is one of the most important process parameters, as this affects the amount of raw material required. Especially for bulk and speciality chemicals, a high yield can significantly improve the overall environmental performance of the product, since the main portion (as much as 90 %) of the total environmental impact usually comes from the production of the raw material (Tufvesson and Börjesson 2008; Adlercreutz 2010).

Enzymes are highly selective catalysts, usually leading to a better use of the raw material and they also work under milder conditions leading to less unwanted by-products being created in the production process (Woodley 2008). Further, when molecules with multiple chiral centres or molecules that contain many functional groups are required, the use of mild enzymatic catalysis often is able to provide a route that avoids protection and subsequent de-protection steps thereby reducing the number of process steps, so-called telescoping. By doing this, the total process yield can be greatly improved and the amount of waste generated can be minimised. Enzymes therefore seem ideally suited for green processes.

2.4.2 Biocatalysis

Life cycle assessments involving the use of enzymes have been performed in a few studies. In Kim et al. (2009a), an LCA of three different pharmaceutical processes using enzymes is presented using GSK's FLASC tool (Curzons et al. 2007). For the production of the actual enzyme catalyst, the media preparation inputs (soybean protein and yeast extract) and immobilisation subprocess were the two major contributors. In the study, the inventory data on raw material is of high quality, also including direct land use change. In a study by Novozymes A/S, the world's largest supplier of enzymes, five different enzymes representing different types of enzymes were reported (Nielsen et al. 2007). The results were of the same magnitude as the GSK study, although some differences were found, mainly due to differences in immobilisation procedure. It can be seen from the abovementioned studies that the contribution of the enzyme to the environmental burden is small compared to the overall environmental contribution from the produced chemical. Therefore we find it acceptable to use generic data from these references instead of making a full calculation of the effects from a specific case. However, these studies are based on optimised production processes where raw material and energy is used effectively and for cases where this would not be so, this needs to be taken into consideration.

2.4.3 Process energy

In several articles, gate-to-gate LCAs of the biocatalytic production process of fatty acid esters have been compared with a conventional process. Several environmental benefits were found, such as energy savings (34–62 %), less waste being created, and also decreased use of solvents and toxic materials (Petersson et al. 2005; Thum and Oxenbøll 2006; Hills 2003; Martinez 2005). However, if the process is analysed from cradle-to-grave, also including the production of the raw material, it can be seen that the contribution from the process is likely to be dwarfed by the contribution from the raw material production (Tufvesson and Börjesson 2008). This is particularly true for bulk and speciality chemicals where the raw material production phase is more energy intensive relative to the process step. For fine chemicals on the other hand, the production process often requires many times more energy than bulk chemicals per tonnes of product. In Wernet et al. (2010), it was concluded that the pharmaceutical ingredient studied had a cumulative energy demand 20 times higher than basic chemical production. Often, around 5–10 % of the total production costs for chemicals come from the process energy (Bieler et al. 2004).

Furthermore, the source of the primary energy is seen to be very important. In Börjesson and Tufvesson (2010), different routes to produce biofuels was examined and in the sensitivity analysis the choice of primary energy used in the conversion plant was evaluated. Depending on the primary energy source (e.g., coal or wood chips), the biofuel sometime preformed even worse than fossil-based fuels.

To conclude, the energy demand in the production process and the source of the primary energy are important to assess, especially for fine chemicals and pharmaceuticals. Inventory data for different primary energy sources is also easily available in literature.

2.4.4 Use of solvents

Organic solvents are widely used in organic synthesis, around 250 to 300 different solvents are available, and the annual consumption is estimated to 4 million tonnes within Europe (Capello et al. 2009). The largest user is the paint industry followed by the chemical industry (Capello et al. 2009). Solvents are preferably avoided and ongoing research into solvent-free organic reactions demonstrates that this could many times be a possibility (Tanaka 2003). Nonetheless, often there is still a great need for the utilisation of solvents for organic reactions and in a life cycle perspective, using a solvent can also lead to higher yield and thereby even an overall improved environmental performance of a product. However, when organic solvents must still be employed, their use needs to be minimised and optimised to enhance the reactions so they have minimal environmental and operational concerns (Gani et al. 2005). A methodology for selecting the most appropriate solvent from an operational and environmental perspective which can also handle multi-step synthesis has been developed by Gani et al. (2005, 2008).

More and more solvents in current use are being identified as having a series of environmental, health and safety challenges and therefore, ‘greener’ substitutes are required (Gani et al. 2008). The use of unconventional solvents to improve the environmental performance of a process has indeed gained much attention. In Sheldon (2005), different reaction media for producing chemicals are presented for instance, water, supercritical carbon dioxide ($scCO_2$) and ionic liquids. In Blowers and Titus (2004), a life cycle inventory on $scCO_2$ was performed identifying the energy use during production as major concern. Ionic liquids, a relatively new type of solvent, are attractive due to their negligible vapour pressure (Anastas and Kirchhoff 2002). However, questions have been raised regarding the toxicity. It is also important to remember that when considering using a benign solvent, full production chain must be considered. For instance, enzymatic processes run using aqueous media often use organic solvents for extracting the product from the reaction media, thereby possibly negating the positive effect. Similarly the use of ionic liquids can complicate the downstream processing of the product because of difficulties to separate the product from the solvent.

For fine chemicals, the use of solvents is often the most crucial parameter affecting the environmental performance of the product. In Jiménéz-Gonzalez et al. (2004), it was concluded that for most of GSK processes, solvents contribute to about 75 % of the total energy usage, about 70 % to the photochemical creation potential (POCP) and about 50 % to the GHG emissions.

Since solvents are a major contributor to the cradle-to-gate life cycle impacts for fine chemicals and pharmaceuticals, the recommendation given is to always included the use of solvents in LCA. Inventory data for different organic solvents are available in literature. In Capello et al. (2009), a life cycle assessment comparing 50 organic solvents produced from petrochemicals, using the Ecoinvent method was presented. In Curzons et al. (1999), 35 solvents commonly used by SmithKline Beecham were studied, including a guide to choose the best solvent. Hellweg et al. (2004) conducted an environmental assessment of 13 different solvents. They concluded that for the production of solvents, the resource consumption contributes significantly to solvents total environmental impacts.

2.4.5 Toxicity and use of toxic material

The release of compounds and metals that represent a threat to human health or biological diversity into the environment pose an increasing threat. Phasing-out of particularly hazardous substances and the minimisation of risks for health and environment associated with the manufacture and use of chemical substances is indeed an issue of outmost importance. However, from a LCA perspective, toxicity is complicated because of the multitude of different chemicals that are used in the chemical industry that have different types of toxic impact on the environment (Baumann and Tillman 2004). For instance, toxicity includes both human and environmental toxicity as well as acute versus long-term effects. For human and eco toxicity, two methods have been developed by BASF (Landsiedel and Saling 2002; Saling et al. 2005).

Even if toxicity cannot always be quantified in an early phase LCA, it is recommendable to at least include a qualitative review of the toxicity of the chemicals that are to be used throughout the life cycle of the product. Standard R-phrases included in all material data sheets can be used as a starting point for the assessment.

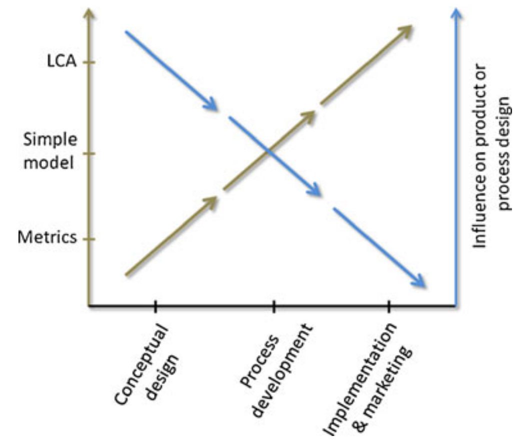

Fig. 1 A sequential approach to evaluate the environmental performance during process development

3 Conclusions

Several articles within the area of green chemistry and biotechnology often promote new techniques or products as ‘green’ or ‘more environmentally benign’ than their conventional counterpart although these articles often do not quantitatively assess the environmental performance. In order to do this, LCA is a valuable methodology. However, on the planning or research stage of a process or product, a full-scale LCA is often too time consuming and complicated. Two reasons for this have been recognised: the method is too comprehensive and it is hard to find inventory data. In this review, key parameters were presented with the purpose to reduce the time-consuming steps in LCA. By providing information on where to focus for different types of chemicals, an adapted LCA could be obtained with a reliable result for the most important key parameters.

In the review, a significant difference in the environmental performance of bulk and fine chemicals was identified. The environmental performance of bulk chemicals are closely connected to the production of the raw material and thereby different land use aspects. Here, a lot can be

learnt from biofuel LCAs. In many of the reviewed articles, focusing on bulk chemicals a comparison regarding fossil and renewable raw material was done. In most of the comparisons, the renewable alternative turned out to be more environmentally preferable than the fossil counterpart, especially for the impact on GWP and energy use. However, some environmental concerns were identified as important to include to assess overall environmental concern regarding renewable recourses, for example eutrophication and the use of land. For fossil platform chemicals, much work on evaluating the environmental performance has been done and data is easily available; there is also a consensus on how to deal with different methodological concerns, for instance allocate the environmental impact between the products.

For fine chemicals and pharmaceuticals, environmental concerns regarding the raw material production is of less importance. For fine chemicals, the production process and environmental aspects connected to this is of greater importance, for example toxicity, solvent use, workers environment and generation of waste. Within the pharmaceutical segment, a lot of products are still based on fossil raw material. Many of the reviewed articles compare biocatalytic production methods with conventional production paths, and several benefits using biocatalysis were found. The high yield achieved when using a more specific catalyst, generating less waste and minimising the amount of raw material needed in the process is the most significant benefit.

It can be concluded that only an approach based on the LCA methodology will give an adequate representation of the environmental performance of a product. However, since this can only be done at a point in the development process where the possibility for changing the process is very limited, there is a need for tools to assess the environmental impact in the early phases of development. Therefore, we suggest that a sequential approach (Fig. 1) should be used through the development process, where a lower level of detail and a higher uncertainty is accepted for initial studies, such as environmental metrics, where different processes are compared on a conceptual basis and a higher accuracy as the number of options is decreased. It should be emphasised that to maximise the accuracy and minimise the time and effort for such studies, it is very important to monitor the parameters that are of most importance for the environmental performance of that specific product or process, which requires a thorough understanding of the process. In this article, we have tried to supply at least part of this understanding. It is also clear that easily accessible and reliable inventory data significantly would help this effort.

4 Future perspectives

As addressed in the editorial by Muñoz (2012), several actions are needed to advance the field of LCA in green chemistry. We believe that to alleviate one of the main bottlenecks simply, more studies assessing the life cycle impact of green chemicals and bio-based chemicals need to become available.

More than this, we hope that more research and discussion will be directed at streamlined methods (and in the future a consensus) and the special challenges for assessing the environmental performance of chemicals in early stage of development.

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